

Preparation of Some Novel Phosphonamidates, Their Phytotoxicity and Herbicidal Properties

Sanjoy K. Das‡ & Nripendra K. Roy*

Division of Agricultural Chemicals, Indian Agricultural Research Institute, New Delhi-110012, India

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Abstract: Fourteen new *O*-phenyl/4-chlorophenyl-*N*-alkyl/aryl-2-chloroethyl phosphonamidates have been prepared and screened for their phytotoxicity towards monocotyledonous (wheat) and dicotyledonous (mustard) plants and herbicidal activity against wild oat. *O*-Phenyl-*N*-propyl-2-chloroethyl phosphonamidate was found to be the most phytotoxic (pre-emergence) and also possessed herbicidal properties. Wheat showed maximum resistance to most of the compounds (post-emergence). *N*-propyl-4-chlorophenyl-2-chloroethyl phosphonamidate was the least active molecule. © 1998 SCI.

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Key words: phosphonamidates; phytotoxicity; wheat; mustard; herbicide; wild oat

1 INTRODUCTION

Organophosphorus compounds are distinguished in the field of pesticide chemistry for their versatility in biological action. At the early stages of development they were known as good insecticides, but their herbicidal activity was discovered much later. Amongst various groups of organophosphorus compounds, phosphonic acid derivatives, viz. phosphonamidates, find a distinct place for their phytotoxic and herbicidal properties on weeds as well as on crop plants. A few known herbicides of this class, e.g., glyphosate and DMPA, have already been commercialised. However, phosphonamidates need more exploration as herbicides. The research in this particular area was first initiated by Khazanchi and Roy,¹ who reported moderate to good herbicidal activity of a series of *O*-methyl dichloromethyl phosphonamidates and diamides. Further, a series of monoamidates and diamidates of 1,1-dichloroethyl phosphonic acid were prepared and screened for their herbicidal and phytotoxic activities along with quanti-

tative structure–activity relationship.² Since phosphonamidates have been shown to be active as herbicides, it is worthwhile to develop more effective herbicides of this group.

This paper deals with the synthesis of two series of phosphonamidates and the study of their phytotoxicity and herbicidal activity.

2 MATERIALS AND METHODS

2.1 Materials

For the syntheses, all the solvents and reagents were dried and purified by either distillation (liquids) or recrystallisation (solids). Thin layer chromatography (on standard silica gel plates) and gas chromatography (HP model 5890A) fitted with FID were used to monitor the reaction and purity of the compound. Characterisation of the synthesised product was done by spectroscopic methods, i.e. PMR (on a Varian EM 360L, 60 MHz) and FT-IR (on a Nicolet 'Impact 400') supported by elemental analyses (on a Perkin-Elmer 2400 C, H, N Analyser).

* To whom correspondence should be addressed.

‡ Present address: Division of Crop Production, IGRI, Jhansi-284 003, India.

2.2 Synthesis

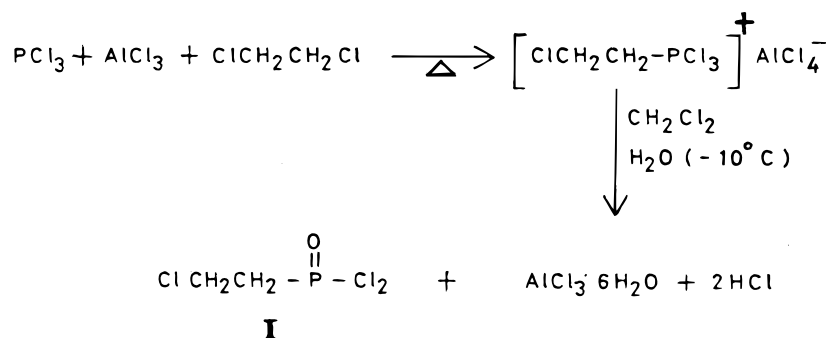
Synthesis of 2-chloroethyl phosphonic dichloride was carried out by a modification of the method of Kinnear and Perren³ by reacting ethylene dichloride, phosphorus trichloride and aluminium chloride in molar ratio under reflux for one hour followed by dilution with methylene chloride and decomposition by water at -10°C . After distilling off the solvent, the acid chloride was distilled off, b.p. 80°C at 10 mm Hg (Fig. 1, Scheme I).

Two series of new phosphonoamidates viz., *O*-phenyl-*N*-alkyl/aryl 2-chloroethyl phosphonamidates and *O*-(4-chlorophenyl)-*N*-alkyl/aryl 2-chloroethyl phosphonamidates, were synthesised using 2-chloroethyl phosphonic dichloride (I), phenol and 4-chlorophenol and seven aliphatic and aromatic amines in 1:1:1 molar ratio. The required quantity of 2-chloroethyl phosphonic dichloride in benzene was taken in a three-necked round-bottomed flask fitted with a mechanical stirrer, a calcium chloride guard tube and a dropping funnel. A mixture of the desired phenol (1 mole) and an equimolar quantity of triethylamine dissolved in benzene was then added to the dichloride from the dropping funnel with constant stirring under ice-cold conditions. Stirring continued for two hours more at

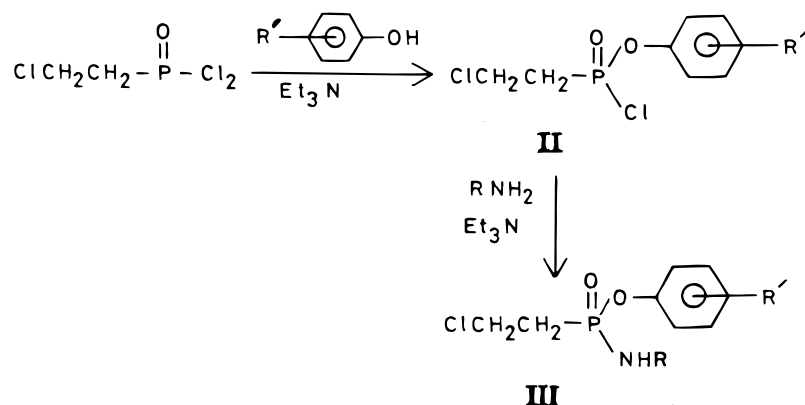
room temperature. The desired amine (1 mole) was then added dropwise with stirring under ice-cold conditions. Finally, the reaction mixture was stirred at room temperature for about two hours more, monitoring the reaction by TLC (solvent system benzene-acetone, 4 + 1 by volume), using iodine as visualising agent. This filtrate obtained after discarding the solid triethylamine hydrochloride precipitate was concentrated by distillation of solvent to give the desired crude product (III). The purification of the crude product was undertaken by either column chromatography (liquids) or recrystallisation (solids) from appropriate solvent (Table 1). The above methods can be envisaged schematically (Fig. 1; Scheme II).

The FT-IR spectra of the compounds showed peaks for P-C stretching vibration, N-H stretching vibration and phosphoryl ($\text{P}=\text{O}$) stretching vibration.⁴ The phosphoryl absorption varied in the range $1196\text{--}1224\text{ cm}^{-1}$. The P-C stretching vibration was found in the range $748\text{--}835\text{ cm}^{-1}$. The N-H stretching vibration was characterised by a peak situated in the range $3132\text{--}3260\text{ cm}^{-1}$ and the peak shape was also variable in nature.

The important chemical shift values and coupling constants in the PMR spectra showed two characteristic signals; first a multiplet corresponding to



Scheme I



Scheme II

Fig. 1. Synthesis of *O*-phenyl/4-chlorophenyl-*N*-alkyl/aryl-2-chloroethyl phosphonamidates.

TABLE 1
Physical and Analytical Data of *O*-Phenyl-*N*-alkyl/aryl 2-chloroethyl Phosphoramidates and *O*-(4-Chlorophenyl)-*N*-alkyl/aryl 2-chloroethyl Phosphoramidates

Compd No.	R in III	R' in III	m.p. (°C)	Yield (%)	Found (%)			Calculated (%)		
					C	H	N	C	H	N
1	C ₃ H ₇	H	Oil ^a	38	50.4	6.6	5.2	50.4	6.5	5.3
2	iso-C ₃ H ₇	H	80	67	50.5	6.8	5.0	50.4	6.5	5.3
3	C ₄ H ₉	H	Oil ^a	43	52.3	6.7	4.9	52.2	6.9	5.0
4	iso-C ₄ H ₉	H	Oil ^a	51	52.3	7.0	4.9	52.2	6.9	5.0
5	C ₆ H ₅	H	108	75	56.6	4.9	5.0	56.8	5.0	4.7
6	4-Cl-C ₆ H ₄	H	111	46	51.5	4.1	4.0	50.9	4.2	4.2
7	4-CH ₃ -C ₆ H ₄	H	72	57	57.9	5.4	4.4	58.1	5.4	4.5
8	C ₃ H ₇	Cl	Oil ^a	42	44.7	5.5	4.6	44.5	5.4	4.7
9	iso-C ₃ H ₇	Cl	85	52	44.5	5.4	4.9	44.5	5.4	4.7
10	C ₄ H ₉	Cl	Oil ^a	41	46.2	5.9	4.6	46.4	5.8	4.5
11	iso-C ₄ H ₉	Cl	Oil ^a	43	46.2	5.7	4.3	46.4	5.8	4.5
12	C ₆ H ₅	Cl	96	60	50.6	4.1	4.1	50.9	4.2	4.2
13	4-Cl-C ₆ H ₄	Cl	84	52	56.2	3.7	3.7	46.0	3.5	3.8
14	4-CH ₃ -C ₆ H ₄	Cl	103	62	52.2	4.7	4.3	52.3	4.6	4.0

^a Column purified.

PCH₂CH₂Cl protons due to α -coupling with phosphorus and the second characteristic signal in the two spectra was a quartet for the PCH₂CH₂Cl protons due to β -coupling with phosphorus atom. The data are compiled in Table 2.

2.3 Bioassay

All the synthesised compounds were tested for their activity against indicator plants, viz., wheat (*Triticum aestivum* L. cv. Kundan) and mustard (*Brassica juncea* (L) Coss. cv. B-9) and also against a weed, wild oat (*Avena sp.*) in plastic pots (15 cm dia. \times 5 cm high)

under closed net-house conditions. Five hundred grams of processed sandy loam soil (Indian Agricultural Research Institute Farm, New Delhi) was placed in each pot. The soil surface in each pot was divided into three compartments, i.e. two for phytotoxicity studies (against crops) and the third for herbicidal activity (against the weed). Fifteen seeds of crops and weed were sown and subsequently the number of plants in each case was reduced to ten by thinning. The plants were watered as and when required. Solutions of test chemicals were prepared at 5000, 2000, 1000, 500 and 250 mg litre⁻¹ in cyclohexanone. One millilitre of each of these solutions was diluted with 9 ml of aqueous solution of 'Tween'-80

TABLE 2
Proton Magnetic Resonance Spectroscopic Data of *O*-Aryl-*N*-alkyl/aryl 2-chloroethyl Phosphoramidates

R in III	R'	Chemical shift δ (ppm)			Coupling constants		
		CH _{α}	CH _{β}	Ar-H	J (Hz) PCCH _{β}	Others	
1	C ₃ H ₇	2.60	3.80	7.30	8	6[NCH ₂ CH ₂ CH ₃]	
2	iso-C ₃ H ₇	2.40	3.90	7.40	8	6[NCH(CH ₃) ₂]	
3	C ₄ H ₉	2.60	3.85	7.30	8	4[N(CH ₂) ₂ CH ₂ CH ₃]	
4	iso-C ₄ H ₉	2.45	3.75	7.25	8	6[NCCCH(CH ₃) ₂]	
5	C ₆ H ₅	2.50	3.70	7.20	8	—	
6	4-Cl-C ₆ H ₄	2.50	3.75	7.15	8	—	
7	4-CH ₃ -C ₆ H ₄	2.50	3.60	6.90	8	—	
8	C ₃ H ₇	2.55	3.70	7.20	8	6[NCH ₂ CH ₂ CH ₃]	
9	iso-C ₃ H ₇	2.30	3.70	7.20	8	4[NCH(CH ₃) ₂]	
10	C ₄ H ₉	2.60	3.80	7.30	8	2[N(CH ₂) ₂ CH ₂ CH ₃]	
11	iso-C ₄ H ₉	2.60	3.80	7.25	8	4[NCCCH(CH ₃) ₂]	
12	C ₆ H ₅	2.70	3.90	7.30	8	—	
13	4-Cl-C ₆ H ₄	2.50	3.80	7.20	8	—	
14	4-CH ₃ -C ₆ H ₄	2.65	3.80	7.10	8	—	

(5 g litre⁻¹) before spraying in one pot. For soil activity studies, the solutions were sprayed uniformly on the soil surface using a hand sprayer. The plants were allowed to grow for 15 days. In the case of foliar activity studies, 15-day-old seedlings were sprayed with different concentrations of the aforesaid test chemicals. The shoot portions of the plants were harvested seven days after spraying. The fresh and dry weights of plant materials from all the treatments were recorded and these were used as parameters to draw the dosage-response curve. The percentage inhibition in both the cases was calculated by the following formula:

$$\text{Inhibition (\%)} = [(C - T)/T] \times 100$$

where *C* and *T* are the growth parameters for the control and the test chemical treatments, respectively. The percentage inhibition for each concentration was converted into probit by using an appropriate conversion table.⁵ The EC₅₀ (concentration of chemical

required for 50% growth inhibition) was derived by plotting the probit values of inhibition against logarithm of the concentration (in mg litre⁻¹), which was the value of concentration corresponding to probit 5.0.

3 RESULTS AND DISCUSSION

The activity of the test chemicals has been evaluated against the monocotyledonous and dicotyledonous plants for soil (pre-emergence) and foliar (post-emergence) application and the significant results have been compared with a reference standard herbicide (anilophos) [Tables 3, 4, 5 and 6].

The most phytotoxic member of the *O*-phenyl-*N*-alkyl/aryl 2-chloroethyl phosphoramidate series was the *O*-phenyl-*N*-propyl derivative, and all other compounds showed better activity against the dicotyledonous plants (mustard) than against

TABLE 3
Phytotoxicity of *O*-Phenyl-*N*-alkyl/aryl 2-chloroethyl Phosphoramidates in Terms of Dry and Fresh Weight Matter^a

	<i>R</i> in III	<i>EC</i> ₅₀ (mg litre ⁻¹) for dry weight matter		<i>EC</i> ₅₀ (mg litre ⁻¹) for fresh weight matter	
		<i>Wheat</i>	<i>Mustard</i>	<i>Wheat</i>	<i>Mustard</i>
1	C ₃ H ₇	1430 (4050)	306 (3430)	1360 (3330)	280 (2450)
2	iso-C ₃ H ₇	2320 (4680)	740 (4760)	2115 (3980)	660 (4220)
3	C ₄ H ₉	2225 (> 8000)	960 (7540)	3030 (> 8000)	1025 (7440)
4	iso-C ₄ H ₉	2740 (> 8000)	1080 (> 8000)	2550 (> 8000)	1230 (7560)
5	C ₆ H ₅	1860 (3597)	840 (2980)	1780 (3440)	730 (3150)
6	4-Cl-C ₆ H ₄	3210 (4948)	990 (3170)	3195 (5110)	1005 (3295)
7	4-CH ₃ -C ₆ H ₄	5315 (> 8000)	940 (3580)	5160 (> 8000)	880 (3720)
	Anilophos	55 (250)	380 (1340)	47 (265)	430 (1460)

^a Data without parentheses are for foliar application and with parentheses are for soil application.

TABLE 4
Phytotoxicity of *O*-(4-Chlorophenyl)-*N*-alkyl/aryl 2-chloroethyl Phosphoramidates in Terms of Dry and Fresh Weight Matter^a

	<i>R</i> in III	<i>EC</i> ₅₀ (mg litre ⁻¹) for dry weight matter		<i>EC</i> ₅₀ (mg litre ⁻¹) for fresh weight matter	
		<i>Wheat</i>	<i>Mustard</i>	<i>Wheat</i>	<i>Mustard</i>
8	C ₃ H ₇	4150 (5115)	1015 (3324)	4410 (5050)	945 (3170)
9	iso-C ₃ H ₇	4580 (6660)	1280 (5350)	4925 (6965)	1165 (5980)
10	C ₄ H ₉	4430 (> 8000)	1390 (> 8000)	4640 (> 8000)	1428 (7930)
11	iso-C ₄ H ₉	5260 (> 8000)	1715 (> 8000)	5450 (> 8000)	1625 (> 8000)
12	C ₆ H ₅	1710 (2586)	740 (2825)	1597 (2425)	697 (3015)
13	4-Cl-C ₆ H ₄	1530 (2033)	324 (2102)	1615 (1870)	310 (2245)
14	4-CH ₃ -C ₆ H ₄	1025 (2090)	312 (1848)	970 (1905)	298 (1730)
	Anilophos	55 (250)	380 (1340)	47 (265)	430 (1460)

^a Data without parentheses are for foliar application and with parentheses are for soil application.

TABLE 5

Herbicidal Activity of *O*-Phenyl-*N*-alkyl/aryl 2-chloroethyl Phosphonamides on the Basis of Dry and Fresh Weight Matter^a

	R in III	EC ₅₀ (mg litre ⁻¹) for wild oat	
		Dry weight	Fresh weight
1	C ₃ H ₇	158 (1060)	112 (970)
2	iso-C ₃ H ₇	510 (1848)	670 (1585)
3	C ₄ H ₉	1090 (4020)	945 (3390)
4	iso-C ₄ H ₉	1325 (6010)	1465 (4415)
5	C ₆ H ₅	930 (2428)	1004 (2334)
6	4-Cl-C ₆ H ₄	1646 (3121)	1530 (3060)
7	4-CH ₃ -C ₆ H ₄	865 (2334)	795 (2297)
	Anilophos	15 (140)	28 (135)

^a Data without parentheses are for foliar application and with parentheses are for soil application.

monocotyledonous plants (wheat). There was a reduction in phytotoxicity with increase in the number of carbon atoms in the alkyl chain. Dicotyledonous plants were, however, more susceptible to foliage application than were monocotyledonous plants; wheat showed maximum resistance to most of the compounds. The *N*-alkyl derivatives of the *O*-(4-chlorophenyl)-*N*-alkyl/aryl 2-chloroethyl phosphonamidate series were found to be less active, whereas the *N*-(4-methylphenyl) derivative was the most active congener. These compounds too showed greater activity towards dicotyle-

TABLE 6

Herbicidal Activity of *O*-(4-Chlorophenyl)-*N*-alkyl/aryl 2-chloroethyl Phosphonamides on the Basis of Dry and Fresh Weight Matter^a

	R in III	EC ₅₀ (mg litre ⁻¹) for wild oat	
		Dry weight	Fresh weight
8	C ₃ H ₇	1650 (3411)	1525 (3213)
9	iso-C ₃ H ₇	1840 (4080)	1810 (3980)
10	C ₄ H ₉	2020 (> 8000)	2140 (> 8000)
11	iso C ₄ H ₉	2550 (7010)	2617 (6730)
12	C ₆ H ₅	725 (2312)	670 (2260)
13	4-Cl-C ₆ H ₄	511 (1997)	575 (1850)
14	4-CH ₃ -C ₆ H ₄	438 (1430)	358 (1490)
	Anilophos	15 (140)	28 (135)

^a Data without parentheses are for foliar application and with parentheses are for soil application.

donous plants (mustard) than to monocotyledonous plants (wheat). The length of carbon chain played a significant role in the structure-activity relationships of both the series. The herbicidal activity of the test compounds in both the series indicated similar trends to those found in phytotoxic activities [Tables 5 and 6]. The most potent herbicidal compound was *O*-phenyl-*N*-propyl 2-chloroethyl phosphonamidate in the first series, while the *O*-(4-chlorophenyl) derivative showed the least activity. On the other hand, in the second series, the *N*-(4-methylphenyl) derivative emerged as the most active herbicidal compound whereas the *N*-alkyl derivatives showed less herbicidal activity. Branching or increase in the length of carbon chain had a negative effect with respect to the herbicidal potency of *N*-alkyl derivatives.

Structure-activity relationship studies of both the series revealed that chlorosubstitution in the phenyl moiety at the *para*-position resulted in a reduction in the activity of phosphonamides containing *N*-alkyl groups, whereas the reverse effect was found in the case of compounds containing *N*-aryl groups. If the same position of the phenyl moiety was substituted by a methyl group, a general reduction of activity was observed. It was also found that substitution of *N* atom by a three-carbon straight chain resulted in good activity in the test compounds; branching of the chain or increase in the chain length beyond three-carbon affected the activity negatively.

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